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Allergic bronchopulmonary aspergillosis and omalizumab

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Allergic bronchopulmonary aspergillosis (ABPA) is most frequently seen in patients suffering from allergic asthma (1). In spite of itraconazole, some patients experience recurrent exacerbations or require long term intensive treatment (steroids) (2). The presence of high levels of IgE, the presence of an often difficult to treat asthma, as well as recent data on the favourable results of the administration of omalizumab in patients with severe asthma (1, 2), prompted the use of omalizumab for ABPA. The aim of the use of omalizumab in this study was to diminish or to discontinue the use of systemic steroid therapy and/or to diminish the number of exacerbations per year in all cases.

Omalizumab in Allergic bronchopulmonary aspergillosis is associated with fewer episodes of exacerbation and reduction of steroids dose.

We recruited 16 patients with ABPA (cystic fibrosis patients were excluded), from nine pneumologists specializing in asthma in French hospitals. None of the patients had previously been treated with omalizumab. The sex-ratio was 8/8. The median age was 56 years (range 29–76 years). Allergic bronchopulmonary aspergillosis was diagnosed 7 years ago (median value, range 4–17 years). All patients had to meet the following diagnostic criteria of ABPA (at the time of the diagnosis of ABPA) (1, 2). Twelve (75%) had bronchiectasis. All had regular follow-up (at least every 6 months) for at least 1 year prior to treatment with omalizumab, and a follow-up of at least 1 year with omalizumab. The median level of total serum IgE was 582 KIU/l (131–3766). The median number of precipitins for AF was 3 (2–8). The median level of specific IgE for AF was 6.7 KIU/l (1.6–73). All patients had in the preceding years been treated with systemic corticoids and 12/16 (75%) had received itraconazole (200 mg/day). Ten out of 16 patients (62%) had three or more exacerbations in the year preceding the onset of treatment with omalizumab. Exacerbation was defined as the need to use oral steroid therapy or of increasing oral steroid therapy. Eight out of 16 patients (50%) required at least one admission to hospital because of exacerbation in the year prior to treatment with omalizumab. Nine patients (56%) had long term treatment with systemic steroids. The median body weight was 75.5 kg (range 57–92). Nine out of 16 patients (63%) had forced expiratory volume (FEV1) < 60% of the predicted value.

Table 1 shows the comparison of the data of the year preceding the onset of treatment with omalizumab, and those of the first year of treatment with omalizumab. Three out of nine patients with long term systemic steroids were able to discontinue this treatment, five reduced the dose to 50% of the initial dose or less, and one has continued with the same dose (10 mg/day) (Fig. 1). Compared to the date of the year preceding the onset of treatment with omalizumab, only two patients suffered three or more exacerbations during the year (Fig. 1). This was observed while with respect to therapeutic adaptation, 10/16 (62.5%) patients were «underdosed» in omalizumab.

At present no moderate or severe side-effects were reported. We report a reduction of the number of exacerbations and of the therapeutic load (systemic steroids) in patients treated by omalizumab suffering from ABPA, without cystic fibrosis. No improvement of the respiratory function was observed. Cases reported in the

Table 1 Evolution of the number of exacerbations, admissions to hospital, systemic corticoid treatment en functional respiratory parameters 1 year before and 1 year after the onset of treatment with omalizumab

Parameters*	Before (–1 year)	After (+1 year)	*P*
Exacerbations	4 (0–12)	0 (0–4)	0.0001
Hospitalisations	1 (0–2)	0 (0–1)	0.03
Systemic steroids (mg/day) in prednisolone equivalents	8.5 (0–60)	0 (0–10)	0.008
FEV1 (%)	53 (33–115)	55 (36–127)	NS
FVC (%)	91 (45–132)	86 (50–137)	NS

FVC, forced vital capacity.

*Expressed as median (range); *P* (significant <0.05).

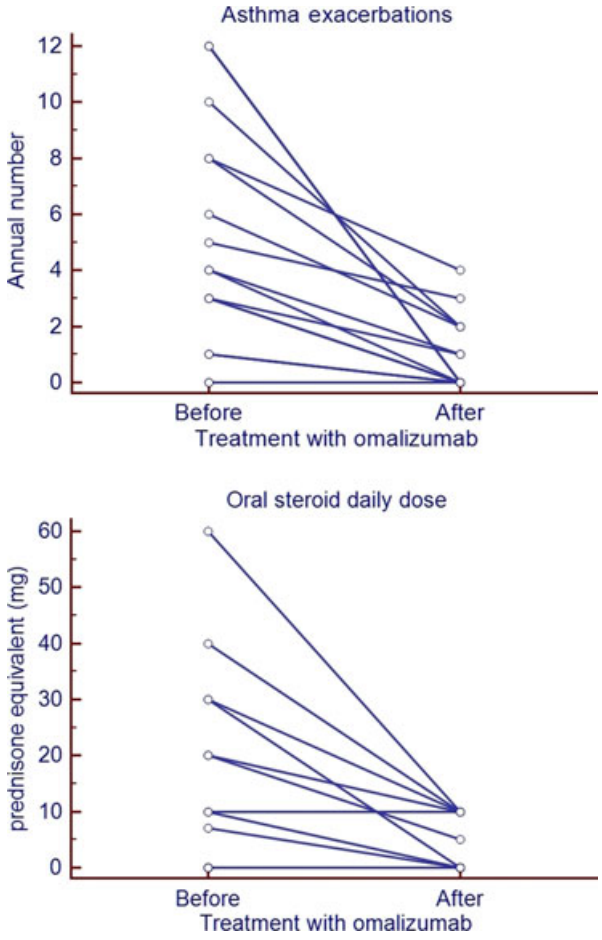

Figure 1 Evolution of exacerbation and the level of oral steroid therapy (prednisolone equivalents) comparing the year before and the year with omalizumab (n = 16).

literature are mainly those of patients suffering from cystic fibrosis with ABPA, treated with omalizumab or a mix of ABPA and aspergillus-induced asthma (3–6). Most treated cases (except one) with a combination of ABPA and cystic fibrosis show a clinical (less exacerbations), therapeutic (less systemic steroids) but also respiratory functional beneficial effect of omalizumab (3–6). The beneficial effects described in these case reports for cystic fibrosis, and the cases presented in this study in adults (apart from cystic fibrosis), warrant a randomised, double blind study of ABPA with a follow-up of at least 1 year.

This study was approved by CEPRO 2010–2014 of the Société de Pneumologie de langue Française (French speaking Pneumology Society).

Conflict of interest

I Tillie-Leblond, C Leroyer, D Dusser, JP Grignet, L Tétu, A Prudhomme and P Germaud have had fee for consulting and for speaking by Novartis.

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